

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP2005/002993

## A. CLASSIFICATION OF SUBJECT MATTER

Int.Cl' A61K45/00, A61K31/51, A61P9/10, A61P43/00, G01N33/15,  
G01N33/50

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Int.Cl' A61K45/00, A61K31/51, A61P9/10, A61P43/00, G01N33/15,  
G01N33/50

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Jitsuyo Shinan Koho	1922-1996	Jitsuyo Shinan Toroku Koho	1996-2005
Kokai Jitsuyo Shinan Koho	1971-2005	Toroku Jitsuyo Shinan Koho	1994-2005

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
CAPLUS (STN), BIOSIS (STN), MEDLINE (STN), EMBASE (STN), WPIDS (STN), JOIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	MASAMURA, K. et al., 'PITAVASTATIN-INDUCED THROMBOMODULIN EXPRESSION BY ENDOTHELIAL CELLS ACTS VIA INHIBITION OF SMALL G PROTEINS OF THE RHO FAMILY.', ARTERIOSCLER.THROMB.VASC.BIOL., (2003), Vol.23, No.3, pages 512 to 517, full text, ABSTRACT, line 26 to 40	1-6, 10, 11 13-15
X A	MORIKAWA, S. et al., 'THE EFFECT OF STATINS ON mRNA LEVELS OF GENES RELATED TO INFLAMMATION, COAGULATION, AND VASCULAR CONSTRUCTION IN HUVEC. HUMAN UMBILICAL VEIN ENDOTHELIAL CELLS.', J.ATHEROSCLER.THROMB., (2002), Vol.9, No.4, pages 178 to 183, full text, ABSTRACT, page 178, left column, lines 1 to 5, DISCUSSION	1-6, 10, 11 13-15

Further documents are listed in the continuation of Box C.

See patent family annex.

- \* Special categories of cited documents:
- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier application or patent but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed
- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "&" document member of the same patent family

Date of the actual completion of the international search  
24 May, 2005 (24.05.05)

Date of mailing of the international search report  
07 June, 2005 (07.06.05)

Name and mailing address of the ISA/  
Japanese Patent Office

Authorized officer

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## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	MCCARTY, MF et al., 'REDUCTION OF SERUM C-REACTIVE PROTEIN BY STATIN THERAPY MAY REFLECT DECREASED ISOPRENYLATION OF RAC-1, A MEDIATOR OF THE IL-6 SIGNAL TRANSDUCTION PATHWAY.', MED.HYPOTHESES, (2003), Vol.60, No.5, pages 634 to 639, full text, ABSTRACT	1-6, 10, 11 13-15
X A	BRANDES, RP et al., 'WITHDRAWAL OF CERIVASTATIN INDUCES MONOCYTE CHEMOATTRACTANT 1 AND TISSUE FACTOR EXPRESSION IN CULTURED VASCULAR SMOOTH MUSCLE CELLS.', ARTERIOSCLER.THROMB.VASC.BIOL., (2003), Vol.23, No.10, pages 1794 to 1800, full text, ABSTRACT	1-6, 10, 11 13-15
X A	WAGNER, AH et al., 'IMPROVEMENT OF NITRIC OXIDE-DEPENDENT VASODILATATION BY HMG-COA REDUCTASE INHIBITORS THROUGH ATTENUATION OF ENDOTHELIAL SUPEROXIDE ANION FORMATION.', ARTERIOSCLER.THROMB.VASC.BIOL., (2000), Vol.20, No.1, pages 61 to 69, full text, ABSTRACT	1-6, 10, 11 13-15
X A	TAKEMOTO, M. et al., 'PLEIOTROPIC EFFECTS OF 3-HYDROXY-3-METHYLGLUTARYL COENZYME A REDUCTASE INHIBITORS.', ARTERIOSCLER.THROMB.VASC.BIOL., (2001), Vol.21, No.11, pages 1712 to 1719, full text	1-6, 10, 11 13-15
X A	ETO, M. et al., 'MODULATION OF COAGULATION AND FIBRINOLYTIC PATHWAYS BY STATINS.', ENDOTHELIUM, (2003), Vol.10, No.1, pages 35 to 41, full text	1-6, 10, 11 13-15
X A	MYSLIWIEC, M. et al., 'STATIN THERAPY-MORE THAN LIPID-LOWERING EFFECT.', ADVANCES IN CLINICAL AND EXPERIMENTAL MEDICINE, (2003), Vol.12, No.2, pages 185 to 190, full text, ABSTRACT, particularly, page 186, left column, line 31 to right column, line 30	1-6, 10, 11 13-15
X A	VECCHIONE, C. et al., 'WITHDRAWAL OF 3-HYDROXY-3-METHYL-GLUTARYL COENZYME A REDUCTASE INHIBITORS ELICITS OXIDATIVE STRESS AND INDUCES ENDOTHELIAL DYSFUNCTION IN MICE', CIRC.RES., (2002), Vol.91, No.2, pages 173 to 179, full text, ABSTRACT, page 173, left column, DISCUSSION	1-6, 10, 11 13-15
X A	DATABASE CAPLUS ON STN, (2002), ABSTRACT NO. 2002-323378 ABSTRACT & CEMERA, M. et al., 'CHOLESTEROL-INDUCED THROMBOGENICITY OF THE VESSEL WALL: INHIBITORY EFFECT OF FLUVASTATIN.', THROMBOSIS AND HAEMOSTASIS, (2002), Vol.87, No.4, pages 748 to 755	1-6, 10, 11 13-15

**INTERNATIONAL SEARCH REPORT**International application No.  
PCT/JP2005/002993**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: 7-9, 12  
because they relate to subject matter not required to be searched by this Authority, namely:  
Claims 7 to 9 and 12 involve embodiments concerning methods for treatment of the human body by therapy and thus relate to a subject matter which this International Searching Authority is not required, under the provisions of Article 17(2)(a)(i) of the PCT  
(continued to extra sheet)
2.  Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

- The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/JP2005/002993

Continuation of Box No.II-1 of continuation of first sheet (2)

and Rule 39.1(iv) of the Regulations under the PCT, to search.

**<Scope of search>**

Claims 1, 4, 10 and 11 relate to a nuclear transfer promoter for Rac protein which comprises, as the active ingredient, a compound defined as having desired properties, i.e., being "an isoprenoid synthesis inhibitor and/or a geranylgeranyl transferase inhibitor". Although these claims involve any compounds having the properties, only small part of the claimed compounds are supported in the meaning within PCT Article 6 and disclosed in the meaning within PCT Article 5.

Although the common technical knowledge at the point of the application is taken into consideration, it is unclear what "an isoprenoid synthesis inhibitor and/or a geranylgeranyl transferase inhibitor" means. Namely, the scope of the compounds having these properties cannot be specified. Thus, the above claims do not comply with the requirement for clearness in the meaning within PCT Article 6 too.

Such being the case, the search was made mainly on the relation between pitavastatin or other statins, which are specifically employed as "an isoprenoid synthesis inhibitor and/or a geranylgeranyl transferase inhibitor" in the description, and the nuclear transfer of Rac protein and blood vessel remedies comprising pitavastatin or other stains as the active ingredient.